5/26 727 25 095

Petition Pursuant to Section 6(b) of the Federal Insecticide, Fungicide, and Rodenticide Act Requesting that the Administrator Conduct a Special Review to Consider Scientific Evidence Demonstrating the Need to Cancel the Registration of the Contraceptive *ZONASTAT-H* for Population Control of America's Wild Horses and Burros

APC 15-0000-92799

Photograph: Friends of Animals

Petition Submitted to the Administer of the United States Environmental Protection Agency

May 19, 2015

Petitioner

~~OPPRESSORS~~
FRIENDS
of ANIMALS

Friends of Animals
Western Region Office
7500 E. Arapahoe Rd., Suite 385
Centennial, CO 80112
720-949-7791

RECEIVED
MAY 28 PM 2:17

~~OPPRESSORS~~
FRIENDS
of ANIMALS

May 19, 2015

Via U.S. Certified Mail

Gina McCarthy, Administrator
U.S. Environmental Protection Agency
Office of the Administrator (1101A)
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Jack Housenger, Director
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

Re: Registration No. 86833-1 (the Unconditional Registration of *Porcine Zona Pellucida* (PZP) under FIFRA Section 3(c)(5) as a Contraceptive to Control Populations of Wild Horses and Burros).

Dear Administrator McCarthy and Director Housenger,

Friends of Animals ("FoA") hereby petitions the U.S. Environmental Protection Agency ("EPA") requesting that the Administrator conduct a special review to consider scientific evidence demonstrating the need to cancel the registration of the contraceptive ZonaStat-H, the primary ingredient of which is *porcine zona pellucida* ("PZP"), for population control of wild horses *(Equus caballus)* and burros *(Equus asinus)* under Section 3(c)(5) of the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"). The registration for PZP (86833-1) was issued to the Humane Society of the United States on or about January 30, 2012.

Pursuant to Section 6(b) of FIFRA, 7 U.S.C. § 136d (b), if new information becomes available to the Administrator that a pesticide, when used in accordance with widespread and commonly recognized practice, generally causes unreasonable adverse effects on the environment, the Administrator may cancel its registration. Here, information is now available to the administrator regarding the unintended (and previously undisclosed) side effects on both the targeted mares and wild horses in general. This new information not only shows unreasonable adverse effects, but also indicates that use of PZP on wild horses likely violates the Free-Roaming Wild Horse and Burro Act ("WHBA"). PZP use is not

needed to comply with any of the population mandates under the WHBA. More importantly, PZP is causing undue physical, social and biological harm to America's wild horses, both individually and collectively; and its continued use may result in genetic bottleneck that can threaten the continued existence of these animals in the wild.

This petition, filed pursuant to 7 U.S.C. § 136(d)(b), 5 U.S.C. § 553(e) and 40 C.F.R. § 154.10, consists of this letter and the attached Statement of Reasons in support of the petitioned action, as well as all documents cited within which are hereby specifically incorporated by reference. FoA specifically requests the Administrator:

1. Conduct a Special Review, pursuant to 40 C.F.R. § 154.1 *et seq.*, to determine whether to initiate proceedings to cancel or reclassify Registration 86833-1;
2. Issue an order suspending Registration 86833-1 pursuant to 7 U.S.C. § 136d(c)(1) during the Special Review and/or proceedings to cancel or reclassify the registration; and
3. Hold a hearing pursuant to 7 U.S.C. § 136(d)(b)(2) to determine if Registration 86833-1 should be canceled or reclassified if it is determined that additional information is needed to act upon this Petition.

Please do not hesitate to contact me at (720) 949-7791 if you need more information. My address appears below and on the cover sheet of the petition.

Sincerely,

Michael Harris
Legal Director
Wildlife Law Program
Friends of Animals
Western Region Office
7500 E. Arapahoe Rd., Ste. 385
Centennial, CO 80112

STATEMENT OF REASONS
IN SUPPORT
OF PETITION PURSUANT TO SECTION 6(B) OF THE FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT REQUESTING THAT THE ADMINISTRATOR CONDUCT A SPECIAL REVIEW TO CONSIDER SCIENTIFIC EVIDENCE DEMONSTRATING THE NEED TO CANCEL THE REGISTRATION OF THE CONTRACEPTIVE *ZONASTAT-H* POPULATION CONTROL OF AMERICA'S WILD HORSES AND BURROS

MAY 19, 2015

Friends of Animals
Western Region Office
7500 E. Arapahoe Rd., Suite 385
Centennial, CO 80112
720-949-7791

A. Introduction.

Reduction of free-roaming horse and burro populations through use of contraception has been a goal of some researchers and animal welfare organizations since the early 1970s (Kirkpatrick, et al., 1990). Various methods have been attempted leading up to the use of PZP. Initially, fertility reduction was demonstrated by using an injectable microencapsulated testosterone propionate (mTP) in stallions which resulted in an 83% decrease in foaling by mares (Kirkpatrick, et al., 1990). Delivery of mTP was done by first immobilizing the stallions and then injecting them. This method of delivery incurred high costs and stress to the animal, resulting in a remote method of delivery. Though mTP was effective in stallions, remote delivery made it difficult to deliver enough steroid to make it effective (Kirkpatrick, et al., 1990).

Another option was tried which also utilized steroid-induced fertility control, but this time the mares were the target animal. The use of ethinylestradiol-progesterone Silastic® implants showed effectiveness, but once again much stress was placed on the target animal because the method of delivery required the mare to be captured, restrained, then undergo field surgery to place the implants peritoneally (Kirkpatrick, et al., 1990).

By 1990, the focus then turned to immunocontraception as an alternative to steroid-induced fertility control. Of primary focus was *porcine zona pellucida* ("PZP"), which is extracted from pig ovaries and is a composite of four different acidic glycoproteins, ZP1, ZP2, ZP3, and ZP4. The antibodies bind to the ZP glycoproteins that surround the egg of the injected animal, alter the glycoproteins' conformation, and block the attachment of sperm, thus preventing fertilization. The principle of efficacy of PZP in horses was first demonstrated by Liu et al. (1989) by inhibiting fertility for seven months in 12 of 14 captive fertile domestic and wild mares. The researchers inoculated the mares with four hand injections of PZP with aluminum hydroxide gel. As the aluminum hydroxide gel was found to be only moderately effective in most of the horses, it was therefore substituted by FCA and FIA (modified Freund's Complete Adjuvant, mFCA, or Freund's Incomplete Adjuvant, FIA) at 2-4 week intervals. A fifth booster injection was administered 6-9 months after the fourth injection. This study also demonstrated that anti-PZP antibody titers of 64% or greater were associated with effective contraception, and that a decline in contraceptive effect correlated with a decline in antibody titers.

On September 16, 2009, the Humane Society of the United States ("Humane Society") submitted an application to the U.S. Environmental Protection Agency ("EPA" or "Agency") for a first registration of ZonaStat-H. The active ingredient in ZonaStat-H is PZP. The requested application use was for the control of wild and feral horse and burro populations on private and public lands. The application proposed that ZonaStat-H be administered to target animals via intramuscular injection in hip or gluteus muscles· either by hand delivery (injection), jab-stick delivery, or remote (dart) delivery. ZonaStat-H consists of an emulsion of two components: (1) the antigen, a naturally occurring, chemically unmodified glycoprotein, PZP; and (2) an adjuvant.

The Agency published a Notice of Receipt for this first registration on January 27, 2010. It was disclosed in this notice that the Humane Society requested waivers for most of the studies ordinarily required from an applicant seeking a pesticide registration, including a toxicity study, ecological effects and environmental fate guideline study, and an efficacy study. The requested waivers were granted by EPA. The Humane Society was allowed to seek its registration based on several studies conducted in the 1990s regarding the efficacy of the drug as a wild horse and burro contraceptive. These studies conclude overall that PZP can be highly effective at reducing fertility rates among wild horses with little to no side effect. A majority of these reviews were published by Dr. Jay Kirkpatrick, a veterinarian that manufactures PZP for use on wild horses. The Humane Society and Dr. Kirkpatrick, however, did not consider the biological, social and behavioral effects the drug can have on wild horses.

Based upon the information provided by the Humane Society, EPA granted the registration on or about January 30, 2012. Since that time, PZP has been in widespread use to control wild horse populations. For example, the Bureau of Land Management, which has jurisdiction over the largest number of wild horse herds on federal public lands, has administered approximately 1944 doses of PZP to wild mares since 2012. *See* BLM, Wild Horse and Burro Fact Sheet (2015). The U.S. Forest Service has also used PZP on mares in the Carson National Forest and potentially elsewhere. Moreover, the use of contraception generally, and the use of PZP specifically, is advocated by the U.S. Geological Survey and the National Academy of Science. (USGS, 2015) (NAS, 2013). These endorsements are directly tied to EPA's grant of the registration to the Humane Society, a group that has long had its own vision of wild horse management based primarily on the use of a drug, PZP, it has championed. *See* HSUS, *Our Vision for Wild Horse Management in the U.S.* (2010).

Petitioners do not challenge EPA's conclusion that "[t]he articles submitted by the HSUS assigned MRID Number 47859801 are acceptable in that they support the efficacy of ZonaStat-H as a contraceptive for the control of wild and feral horses and burros." However, research has now demonstrated changes in mare stress and reproductive physiology, in addition to changes in male behavior. For example, researchers now know that:

- Mares which change groups more often (such as those treated with PZP) can exhibit increased stress levels and that this increased stress is maintained for at least two weeks after the group changes occur (Nuñez, Adelman et al., 2014);
- Mares that receive PZP over extended periods are more likely to cycle, become pregnant, and subsequently give birth in the fall (Nuñez, Adelman et al., 2010) and winter (unpublished data) months. This is significant because offspring born at this time face nutritional and thermoregulatory challenges not experienced by their counterparts born during the normal foaling season (during the spring and summer), potentially making developmental benchmarks difficult to achieve (Sadleir, 1969);
- After contraception management, PZP recipients both attract and initiate more instances of reproductive behavior (Nuñez, Adelman et al., 2009) and are more

often the harem male's nearest neighbor during the fall and winter (Nuñez, 2011), indicating that group spreads are reduced. These changes can be important as horses typically spread out in the fall and winter months to find scare forage. Such changes represent an increase in energy expenditure and a potential decrease in nutrient intake during a time of year when sufficient energy reserves are at a premium (Sadleir, 1969);

- Mares treated for more consecutive years are more likely to exhibit the behavioral and physiological changes outlined above (Nuñez, Adelman et al., 2010), decreases in ovarian function, and perhaps, permanent infertility; and
- Where, as is often the case, the plan is to vaccinate non-reproductive females (those between 1 and 3 years old), it will preclude young mares from forming the important social attachments between males and females typically made when foals are conceived. Such changes could further affect herd dynamics (Nuñez, 2014).

This new information demonstrates that PZP generally causes unreasonable adverse effects on the environment which warrants the Agency's consideration as to whether to cancel or reclassify its registration of this pesticide as a method of controlling wild horse and burro populations. Specifically, PZP poses the risk of immediate physical damage to the dosed mares, can increase the mortality rate in foals born to treated mares after the PZP loses its effectiveness, can result in social disruptions among herds with treated mares that can damage long-term herd cohesion that is critical to the health of the animals, and places the wild horses at risk of a genetic bottleneck. None of these risks were considered as part of the pesticide's initial registration.

B. Legal Authority.

1. Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

The Administrator of the EPA may issue a notice of cancellation of a pesticide when the pesticide, when used in accordance with widespread and commonly recognized practice, causes unreasonable adverse effects on the environment. 7 U.S.C. § 136d(b) (2015). *Defenders of Wildlife v. Jackson*, 791 F. Supp. 2d 96, 102 (D.D.C. 2011); *Reckitt Benckiser, Inc. v. EPA*, 613 F.3d 1131, 1134 (D.D.C. 2010). This authority is discretionary, but if the Administrator refuses to commence the cancellation proceedings, the party requesting the cancellation has a right to demand a hearing in a Federal Court of Appeals outside the administrative agency. *Defenders of Wildlife*, 791 F. Supp. 2d at 102; *Reckitt Benckiser, Inc.*, 613 F.3d at 1134.

The phrase "unreasonable adverse effects on the environment" is defined within FIFRA as "any unreasonable risk to man or the environment, taking into account economic, social, and environmental costs and benefits of the use of any pesticide." 7 U.S.C. § 136(bb)(1) (2015). Cases applying this definition affirm the statutory language straightforwardly, quoting the definitional language within FIFRA. *Chem. Specialties Mfrs. Ass'n v. United States EPA*, 484 F. Supp. 513, 515-16 (D.D.C. 1980) (quoting 7 U.S.C. § 136(bb)(1)). The statute's language and its surrounding case law necessitate Administrative discretion because the statute specifically requires that the Administrator

balance the risks and benefits of continued registration of the pesticide. *Id.* at 516. Therefore, the EPA is empowered through FIFRA to make the ultimate determination, upon new evidence, that a substance registered as a pesticide poses such an unreasonable risk of adverse effect to the environment. *See Ciba-Geigy Corp. v. EPA*, 874 F.2d 277, 280 (5th Cir. 1989) (holding that FIFRA gives the EPA Administrator significant discretion to determine that possible bird kills are an unreasonable adverse effect despite the fact that they do not actually significantly reduce the bird population, and that cancellation proceedings are proper); *Envtl. Def. Fund v. EPA*, 510 F.2d 1292, 1297 (D.C. Cir. 1975) (holding that the EPA Administrator has broad discretion to make decisions regarding policy related to the public interest).

EPA, by regulation, has established a "Special Review" process to assist in determining whether to initiate procedures to cancel or reclassify the registration of a pesticide because that the pesticide may cause unreasonable adverse effects on the environment. 40 C.F.R. § 154.1. According to the regulations:

> The process is intended to ensure that the Agency assesses risks that may be posed by pesticides, and the benefits of use of those pesticides, **in an open and responsive manner**. The issuance of a Notice of Special Review means that the Agency has determined that one or more uses of a pesticide **may** pose significant risks and that, following the completion of the Special Review process, the Agency expects to initiate formal proceeding seeking to cancel, deny, reclassify, or require modifications to the registration of the product(s) in question unless it has been shown during the Special Review that the Agency's initial determination [in the Notice of Special Review] was erroneous, that the risks can be reduced to acceptable levels without the need for formal proceedings, or that the benefits of the pesticide's use outweigh the risks.

Id. (emphasis added).

The determination to issue a Notice of Special Review may be based, among other things, upon a validated test or other significant evidence that the use of the pesticide in question: (a) may result in residuals in the environment of nontarget organisms at levels which equal or exceed concentrations acutely or chronically toxic to such organisms; (b) may pose a risk to the continued existence of any endangered or threatened species under the Endangered Species Act; or (c) may otherwise pose a risk to the environment which is of sufficient merit to determine whether the use of the pesticide offers offsetting social, economic, and environmental benefits to justify its continued use. *See* 40 C.F.R. § 154.7.

The Administrator may consider whether to issue a Notice of Special Review on her own initiative or at the suggestion of any interested party.[1] 40 C.F.R. § 154.10. In making a

[1] Although the regulations are silent as to the form such a "suggestion" must or should take, the Administrative Procedure Act ("APA") provides that "[e]ach agency shall give an interested person the right to petition for the issuance, amendment, or repeal of a rule." 5

determination on whether to issue a Notice of Special Review, the Administrator shall be guided by:

> The principle that the **burden of persuasion** that a pesticide product is entitled to registration or continued registration for any particular use or under any particular set of terms and conditions of registration **is always on the proponent(s) of registration**.

40 C.F.R. § 154.5 (emphasis added). Thus, in order to be entitled to a Special Review, a petitioner need only present *prima facie* evidence to the Administrator that the pesticide in question causes unreasonable adverse effects on the environment. Once the petitioner presents a facial case that cancelation or reclassification of a registration might be warranted, the burden to demonstrate otherwise shifts to the proponents of registration. *Envtl. Def. Fund v. EPA*, 548 F.2d 998, 1004 (D.C. Cir. 1976).

2. Wild Free-Roaming Horses and Burros Act ("WHBA").

Modern horses, zebras, and asses belong to the genus *Equus*, the only surviving genus in a once diverse family, *Equidae* (Kirkpatrick and Fazio, 2010). Based on fossil records, the genus *Equus* originated in North America about three to four million years ago and spread to Eurasia by crossing the Bering Land Bridge two to three million years ago. A great deal of paleontological data has led experts to estimate that the modern horse, *E. caballus*, originated about two million years ago in North America (Kirkpatrick and Fazio, 2010). The last North American extinction probably occurred between 11,000 and 13,000 years ago (Kirkpatrick and Fazio, 2010), although more recent extinctions for horses have been suggested (Haile, et al., 2009). The expansion of humans across the Bering Land Bridge has been suggested as a possible explanation for the extirpation of wild horses in North America 11,000 to 13,000 years ago (Harrington, 2002). Climate change and changes in North American vegetation also likely played a role (Hulbert, 1993; Sharp and Cerling, 1998). Had it not been for previous westward migration into northwest Russia and Asia, the horse would have faced complete extinction. Fortunately, horses did survive, and spread to nearly every continent (Kirkpatrick and Fazio, 2010).

In the mid-1500s, Spanish conquistadors brought horses with them to North America, and some escaped or were released from captivity onto western rangelands (Garrott and Oli, 2013). These horses eventually developed distinct behaviors from their domestic counterparts. The fact that horses were domesticated before they were reintroduced matters little from a biological or behavioral viewpoint, as the reintroduced species is identical to that which had formerly been eliminated (Kirkpatrick and Fazio, 2010).

U.S.C. § 553(e). Under the APA, the term "rule" means the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy . . . ." 5 U.S.C. § 551(4).

By 1900, there were two to seven million wild horses in the United States (Ryden, 1999; Thomas, 1979). However, the population began declining in the early 1900s due to human exploitation. In the 1920s, well over one hundred thousand horses were slaughtered and sold for chicken feed, pet food, and human consumption (McKnight, 1959). Furthermore, hunters and ranchers started killing wild horses and driving them off the land based on the belief that wild horses would damage the land or compete with commercial livestock grazing (Ryden, 1999).

It was not clear that there were too many horses, nor that the horses were actually damaging the land. Nonetheless, the United States Forest Service and the United States Grazing Service (the predecessor to the BLM) responded to pressure from ranchers by removing tens of thousands of wild horses from federal property and allowing people to poison water holes and slaughter them without limit (Cruise and Griffiths, 2010). As part of the plan to clear the range of wild horses, the government collaborated with rendering plants that paid hunters six cents per pound to remove horses (Cruise and Griffiths, 2010). According to one BLM official, "within a period of four years [1946 to 1950] [BLM] removed over 100,000 abandoned and unclaimed horses from Nevada ranges." (Cruise and Griffiths, 2010 p. 59). Officials estimated that fewer than 4,000 horses remained in Nevada by 1950 (Cruise and Griffiths, 2010 p. 60).

Many people, outraged at the practice of violently and systematically eliminating wild horses, encouraged Congress to pass the Hunting Wild Horses and Burros on Public Lands Act in 1959 (Ryden, 1999). The Act banned the hunting of wild horses on federal land from aircraft or motorized vehicles. 86 P.L. 234, 73 Stat. 470. After passage of this law, however, ranchers and others continued to sell and slaughter wild horses (Cruise and Griffiths, 2010).

In 1971 Congress passed the WHBA, 16 U.S.C. §§ 1331 *et seq.*, and found that, "wild free-roaming horses and burros are living symbols of the historic and pioneer spirit of the West; that they contribute to the diversity of life forms within the Nation and enrich the lives of the American people; and that these horses and burros are fast disappearing from the American scene." Upon finding this, Congress stated its policy was that "wild free-roaming horses and burros shall be protected from capture, branding, harassment, or death, and to accomplish this they are to be considered in the area where presently found as an integral part of the natural system of public lands." 16 U.S.C. § 1331.

WHBA requires BLM to "protect and manage wild free-roaming horses and burros as components of the public lands . . . in a manner that is designed to achieve and maintain a thriving, natural ecological balance on the public lands." 16 U.S.C. § 1333(a). Additionally, WHBA requires management of wild horses and burros to be at "the minimal feasible level." *Id.* To do so, for each herd management area ("HMA") , BLM must: (1) maintain a current inventory of wild horses in the management area, (2) "determine [the] appropriate management level" of wild horses that the HMA can sustain, and (3) determine the method of achieving the designated management level and managing horses within it. 16 U.S.C. § 1333(b)(1); 43 C.F.R. §§ 4710.2, 4710.3-1. An appropriate management level, according to BLM's Wild Horses and Burros Management Handbook, is "expressed as a population range

within which [wild horses] can be managed for the long term" in a given HMA without resulting in rangeland damage.

Lastly, WHBA requires BLM to make a determination that there are excess wild horses prior to gathering or removing any wild horses from the range. *See Colorado Wild Horse & Burro Coal., Inc. v. Salazar*, 639 F. Supp. 2d 87 (D.D.C. 2009). WHBA defines the term "excess" as animals that "must be removed from an area in order to preserve and maintain a thriving ecological balance and multiple-use relationship in that area." 16 U.S.C. § 1332(f). BLM's Wild Horses and Burros Management Handbook explains that: "Before issuing a decision to gather and remove animals, the authorized officer shall first determine whether excess [wild horses] are present and require immediate removal. In making this determination, the authorized officer shall analyze grazing utilization and distribution, trend in range ecological condition, actual use, climate (weather) data, current population inventory, wild horses and burros located outside the HMA in areas not designated for their long-term maintenance and other factors such as the results of land health assessments which demonstrate removal is needed to restore or maintain the range in a [thriving, natural ecological balance]."

C. *Prima Facie* Evidence That Warrants a Special Review Process.

Although the information regarding PZP used to support its registration in 2009—studies that almost all took place before 2010—is generally accurate regarding PZP efficacy, with regards to ecological and environmental effects it is outdated now. Recent research has demonstrated changes in mare stress and reproductive physiology, in addition to changes in male behavior. For example, we now know that mares which change groups more often (such as those treated with PZP) can exhibit increased stress levels and that this increased stress is maintained for at least two weeks after the group changes occur (Nuñez, Adelman et al., 2014). Short-lived stressful situations are commonplace for several species (Sapolsky, 2005); however, repeated increases in stress hormones can adversely affect cardiovascular and immune function and, in the most extreme cases, can result in adverse neurobiological effects (Sapolsky, 2005). In addition, recent research shows that PZP: (1) can cause irreversible physical damage to the treated mares; (2) can increase mortality of offspring post-PZP effectiveness; (3) can result in social disruption among herds with treated mares that can result in long-term herd disintegration; and (4) can create a genetic bottleneck that may ultimately extinguish the population as a whole.

1. PZP can cause irreversible physical damage to the treated mares.

Physical effects of PZP in the short term are ostensibly non-existent. But with repeated applications, researchers have continually discovered, the mares often experience ovulatory failure and permanent infertility. Even on Assateague Island, arguably the most publicized management success story, the mares treated over multiple birthing seasons often eventually experience ovulatory failure (Ransom, et al., 2013). In another study, researchers explored further and discovered that ovulation failure experienced by these horses correlates with only five to seven years of PZP treatment, directly contradicting the drug's apparent "reversibility" (Nuñez, et al., 2010). This timeframe for ovulatory failure corresponds to other studies' findings of decreased fertility in post-treated females. Even

after population managers have discontinued the PZP treatment in a given animal, the wild mares remain 38.5% less likely than their untreated counterparts to become pregnant in subsequent years (Ransom, et al., 2013). Other research has even shown that PZP's efficacy, upon initial treatment, is 97%, dropping to 87% between years one and five, and finally reaching 100% "after five or more consecutive applications," and even after the applications have ceased (Nuñez, et al., 2010). This is contrary to the assertion of its reversibility, as only five years of treatment is required to render the mare permanently infertile.

The ability of mares to become pregnant after treatment is dependent upon the number of consecutive treatments received. Mares treated for more consecutive years are more likely to exhibit the behavioral and physiological changes outlined above (Nuñez, Adelman et al., 2010), decreases in ovarian function (Kirkpatrick, Liu et al. 1990), and perhaps, permanent infertility. Shackelford mares for which treatment was halted in 2009 have yet to return to pre-contraception levels of fertility (Nuñez, 2014, unpublished data, see Figure 1). This effect is exacerbated in mares that received more consecutive treatments (Nuñez, 2014, unpublished data).

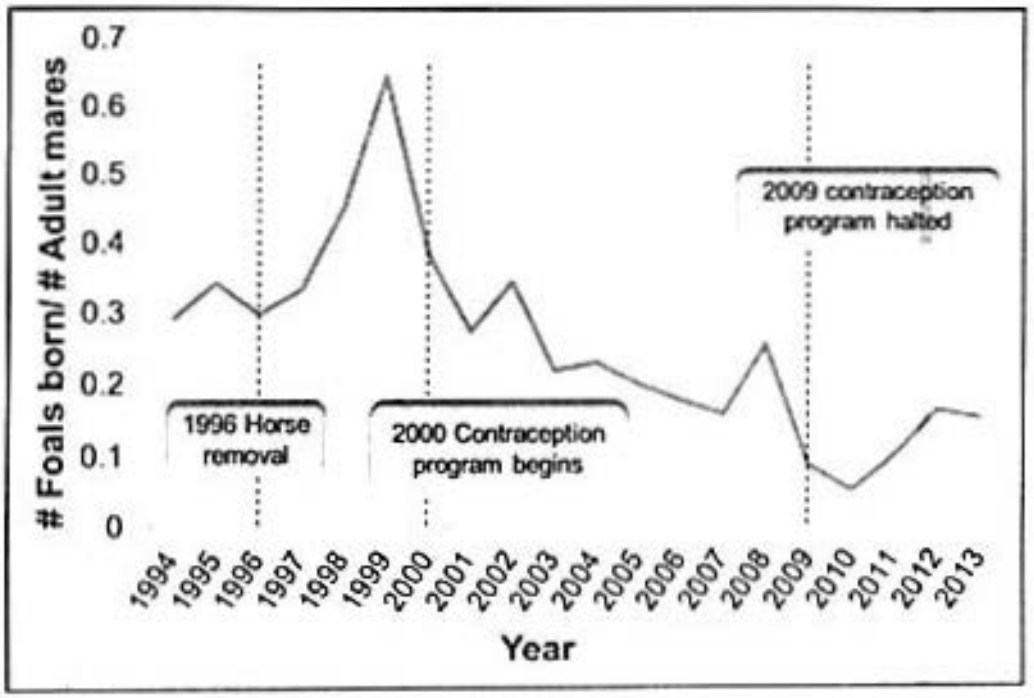

Figure 1. Pregnancy in Shackleford mares before, during and after contraception management.

2. PZP can increase mortality in foals post-PZP effectiveness.

When PZP is introduced into wild horse populations, it tends to have a cascading effect on the timing of conception and foaling in PZP treated mares (Liu, et al., 1989; Ransom, et al., 2014; Nuñez, et al., 2010; Madosky, et al., 2010). Jason Ransom's 2013 study found that large mammals, such as wild horses, breed according to seasonal cues like temperature and the amount of sunlight the animal is exposed to, or "photoperiod" (Ransom, et al., 2013). In the case of wild horses, these environmental factors result in

mostly springtime births, coinciding with peak forage availability (Ransom, et al., 2013). The abundance of forage is critical to meet the increased trophic needs of nursing mares and new foals (Ransom, et al., 2013). Births occurring at other times of the year, after forage availability has begun to decline, result in increased foal mortality. Ransom et al. found that the foals' chances of mortality increased 1.4% for every ten days after peak forage that birth occurred (2013). This may seem insignificant, but for foals born 180 days after the summer solstice (roughly around the winter solstice), the risk of mortality increases over 25%. Even if the foals survive their disadvantage, the reduction in forage availability can prevent them from reaching critical developmental milestones (Nuñez, et al., 2010). Mares birthing at times off the peak forage availability results in negative health outcomes for their foals, including developmental delays, as well as death. Mares treated with PZP are more likely to birth asynchronously with peak forage, making maternal treatment with PZP a major contributor to negative foal outcomes.

If the PZP vaccination is ineffective, or has lapsed, and the mare conceives, the foal has a greater likelihood of being born off of peak foraging times (Nuñez et al., 2010; Madosky et al 2010). The nearly yearlong gestation of the horses means that the breeding period occurs slightly before the summer solstice; foals conceived during this period are born approximately two to four weeks before the next summer solstice (Ransom, et al., 2013; Nuñez, et al., 2010). This is the ideal time for foals to be born because it corresponds with peak forage availability (Ransom, et al., 2013). The PZP, however, contributes to increased reproductive behaviors both from and towards the treated mares at suboptimal times of the year (Ransom, et al., 2010). For example, mares failing to conceive at or around the solstice will continue to exhibit reproductive behaviors well after forage has begun to decline. This increases the likelihood that a foal would be conceived, and therefore born, at a suboptimal time of the year (Ransom, et al., 2013). Without the trophic support of abundant forage, the likelihood of these foals' deaths is quantifiably increased as they are born later after the peak forage of the summer solstice (Ransom, et al., 2013).

It is true that other variables do affect the foals' survival, but all of the other variables are compounded by PZP treatment of females within the herd; none of them have the same detrimental effect as they do when they are compounded with PZP treatment (Ransom, et al., 2013). Furthermore, despite the existence of the other variables, the most significant variable to survival of foals born in later months is PZP treatment (Ransom, et al., 2013).

3. Herd cohesion is critical to the health of the horses, and interfering with the ability to bear foals damages that cohesion.

Wild horses organize themselves into herds or harems consisting of usually one lead stallion, one to several mares, and the herd's juvenile offspring (Nuñez et al 2009). The herd is generally socially stable, with each core adult remaining with the group for months or years (Nuñez, et al., 2009). In order for the herd to remain stable, however, each adult must remain within it; changes to the structure, which are typically rare, will disrupt the herd's stability, bringing with it elevated stress responses for many horses involved (Nuñez, et al., 2009). Stable herds also tend to correlate with increased foal survival (Madosky, et al., 2010). Overall, herd cohesion is vital to the health of the animals.

Multiple studies have shown that the most significant factor in maintaining herd cohesion is foal presence and pregnancy (Nuñez, et al., 2009; Madosky, et al., 2010). Mares who are pregnant or lactating tend to remain in their herds, while mares treated with PZP change herds and visit other herds more frequently (Madosky et al 2010). Changes to herd composition disrupts the normal social structure of the entire wild horse population necessarily; of course a mare's unsettled wandering affects not only the herd she abandons, but also the herd she joins (Madosky, et al., 2010). This disruption is felt throughout a wild horse population, especially when a majority of the mares within that population are treated with PZP (Madosky, et al., 2010; Ransom, et al., 2014; Nuñez, et al., 2009). It would not be just one mare traveling around to different herds, but could realistically be virtually all the mares, essentially destroying the social structure of the population and causing elevated stress levels to all the animals therein. Madosky's study indicates that PZP has a significant effect on mares' wandering, finding that the contracepted mares are 40% more likely to change herds than their non-contracepted counterparts (Madosky, et al., 2010). Another study specifically shows that herd fidelity negatively correlates with PZP application: as more horses are treated, the less faithful they are to the herd in which they normally live (Ransom, et al., 2014). In short, the herd disruption caused by PZP places wild horses at risk of reproductive failure (which as noted below can be another factor leading to a genetic bottleneck).

Stress to wild horses causes sustained elevated cortisol levels, which can be extremely physiologically damaging (Nuñez, et al., 2014). This stress can cause a multitude of adverse physical effects, including negative impacts to cardiovascular function, inhibition of reproduction, compromised immune response, and neurological issues (Nuñez, et al., 2014). Nuñez' study finds that mares transferring herds exhibit elevated cortisol levels for two weeks after their herd transfer, at levels not similarly exhibited in mares who remain with their herds (Nuñez, et al., 2014). For mares that change herds frequently, these stress levels can be elevated constantly. Elevated stress response to transferring herds also causes increased offspring mortality and increased parasite loads (Nuñez, et al., 2014). These effects impact the physical health of the horses, and because the effects are so widespread, these impacts can be felt throughout the wild horse populations.

4. Preventing some mares from producing foals can create a genetic bottleneck that may ultimately extinguish the population as a whole.

Prevention of reproduction can have significant genetic effects on the wild horse populations, in addition to the physical and social effects. First, by limiting the number of mares that are permitted to reproduce, managers limit future generations' genetic diversity. A similar problem occurred in the elephant seal population in the mid 1800s (Bonnell and Selander, 1974). Hunted to near extinction, an extremely small population in a small refugium of elephant seals remained, from which practically all extant elephant seals today descend (Bonnell and Selander, 1974). This dramatic reduction in population, followed by a population boom, created what is known as a "bottleneck" (Bonnell and Selander, 1974). While a genetic bottleneck does not necessarily eliminate a population, it often will exert pressure on the population that can reduce genetic fitness (Dunn and Byers, 2008). In a classic bottleneck situation inbreeding between individuals reduces the

long-term viability of the population (Heber and Briskie, 2010). Using immunocontraception on wild horse populations is not a classic bottleneck because the contracepted individuals remain within the population. But by controlling the fertility of a significant portion of the adult females, the same effect is achieved; only a few individuals are available to pass on their genes, ensuring that the next generation has significantly reduced genetic diversity than it would have had if immunocontraception had not been applied. If all of the members of a wild horse population are descended from the same few mares, eventually inbreeding will reduce the fitness of the population beyond the point of viability, potentially extinguishing the entire population.

Another genetic effect becomes apparent upon consideration of the fact that PZP works by stimulating the horse's own immune system into preventing fertilization of the egg (Ransom et al 2014). The drug is not 100% effective because not every mare's immune system is sufficiently responsive (Ransom, et al., 2014; Nuñez, et al., 2009). It is the mares with weaker immune systems that continue to pass on their genes; mares with the strongest immune systems are effectively contracepted (Ransom, et al., 2014). This may result in the prevention of strong immune systems from reproducing, and may destroy the ability of the wild horse in general to fight off infection in the future. This result could render the whole population sickly and frail and contribute to the population's possible extinction (Ransom, et al., 2014).

D. Regulatory Basis for Initiation of a Special Review.

1. PZP can result in residues in the environment of nontarget organisms—the foals of treated mares conceived and birthed post application—that equal or exceed concentrations that are toxic to those organisms.

In granting the Humane Society's waiver requests to fulfill the required ecological effects and environmental fate guideline studies, EPA determined that "[e]xposure to non-target organisms is not likely to occur because of the targeted nature of the application." Assuming that the targeted organism is the wild mare that is dosed with PZP, then given new information generated since Humane Society's 2009 application, this statement can no longer hold true. As discussed above, after the administered PZP is no longer effective to prevent conception, the drug's residual effect: (a) contributes to increased reproductive behaviors at suboptimal times; (b) increases the likelihood that birth will also occur at suboptimal times; and (c) and quantifiably increases the likelihood of the foal mortality. While it is true that PZP is not directly killing foals conceived post-PZP effectiveness (i.e., it is not poisoning the foal), residual PZP in the foal's pre-birth environment (its mother) is the reason for the increased mortality rate. Moreover, an increased mortality rate of up to 25% is significant. Petitioner has presented a *prima facia* case for initiating a Special Review based upon this consideration.

2. PZP may otherwise pose a previously undisclosed risk to the environment which is of sufficient magnitude to merit a Special Review.

Congress declared that "wild free-roaming horses and burros are living symbols of the historic and pioneer spirit of the West; that they contribute to the diversity of life forms within the Nation and enrich the lives of the American people; and that these horses and burros are fast disappearing from the American scene." Moreover, "they are to be considered in the area where presently found as an integral part of the natural system of public lands." In other words, wild horses are part of the western landscape and environment. Recent studies indicate that the use of PZP as a population control tool poses multiple risks to these animals that were never disclosed or considered during the FIFRA registration process. Whether it is physical damage to dosed mares, the increased mortality in foals born to previously treated mares, the disruption of herd cohesion that is critical to the health of the horses individually and as a herd, or the increased risk of a genetic bottleneck, PZP (even after just a couple of years of widespread use) poses a significant risk to these animals. Petitioner has presented a *prima facia* case for initiating a Special Review based upon this consideration.

3. The use of PZP violates the WHBA.

While the Agency's regulations only identify risk to species protected by the federal ESA as a specific criteria for initiation of a Special Review, wild horses and burros are protected by a species-specific act that seeks to protect them in ways similar to the ESA. Thus, Congress has declared that "wild free-roaming horses and burros shall be protected from capture, branding, **harassment, or death**, and to accomplish this they are to be considered in the area where presently found as an integral part of the natural system of public lands." Certainly, it is in the spirit of the regulations and FIFRA to consider whether a pesticide could violate a species-specific act when considering whether to initiate proceedings to cancel or reclassify the pesticide's registration. In this regard, new studies indicate that PZP use is harassing, and even killing, wild horses in ways not considered as part of the initial registration process. While it is true that the WHBA provides for an exception from these general mandates to protect wild horses in order to control their populations, this exception is both narrow (the animal must be deemed "excess") and can only be applied if the implementing agency (BLM or USFS) first completes certain statutory requirements. It may be that with regard to the decision to dose a particular mare the implementing agency can comply with the WHBA. However, the other horses in the herd that are not dosed with PZP (as well as the unborn foals) cannot be legally defined as "excessive" and, thus, the harassment or death to these animals caused by PZP violates the WHBA.

E. Conclusion.

Wild horses are not only a living embodiment of the spirit of the American West, but are also an important part of the ecosystem in which they live. The application of PZP to control wild horse fertility has long-term consequences that are already occurring, and will continue to occur, specifically reduction in the genetic fitness and viability of these majestic

and ecologically critical creatures. In order to preserve the wild horse population and the environment of the American West, the EPA Administrator should proceed with a Special Review to consider whether there are grounds to initiate proceedings to cancel or reclassify this insidious pesticide.

Sources

Bonnell, M.L., & Selander, R.K. (1974). Elephant Seals: genetic variation and near extinction. Science, 184, 908-9.

Bureau of Land Management. (2015). Wild Horse and Burro Quick Facts.

*Cruise, D., & Griffiths, A. (2010). Wild Horse Annie and the Last of the Mustangs: The Life of Velma Johnston. Simon and Schuster.

*Downer, Craig C. (2014). The Wild Horse Conspiracy.

Downer, Craig C. 2014. The horse and burro as positively contributing returned natives in North America *American Journal of Life Sciences* 2014; 2(1): 5-23.

Dunn, Stacey A., & Byers, John A. (2008). Determinants of Survival and Fecundity through a Population Bottleneck in Pronghorn. Oxford Journals.

Garrott, R. A., & Oli, M. K. (2013). A Critical Crossroad for BLM's Wild Horse Program. Science, 341(6148), 847-848.

Haile, J., Froese, D. G., MacPhee, R. D., Roberts, R. G., Arnold, L. J., Reyes, A. V., ... & Willerslev, E. (2009). Ancient DNA reveals late survival of mammoth and horse in interior Alaska. Proceedings of the National Academy of Sciences, 106(52), 22352-22357.

Harington, C. R. (2002). Yukon horse. Beringian Research Notes, 14.

Heber, Sol, & Briskie, James V. (2010). Population Bottlenecks and Increased Hatching Failures in Endangered Birds. Conservation Biology.

Hulbert Jr, R. C. (1993). Taxonomic Evolution in North American Neogene Horses (Subfamily Equinae): The Rise and Fall of and adaptive Radiation. Paleobiology, 216- 234.

Humane Society of the United States. (2010). The HSUS and Our Vision for Wild Horse Management in the U.S.

Kirkpatrick, J. F., & Fazio, P. M. (2010). Wild horses as native North American wildlife. Retrieved from The Science and Conservation Centre. Accessed April, 28, 2010.

Kirkpatrick, J.F., Liu, I.K.M., Turner, John W. (1990). Remotely Delivered Immunocontraception in Feral Horses. Wiley.

Liu, I.K.M., Bernoco, M., Feldman, M. (1989). Contraception in Mares Heteroimmunized with Pig Zonae Pellucidae. Journal of Reproductive Fertility.

Madosky, Jessa M., Rubenstein, Daniel I., Howard, Jerome J., Stuska, Sue. (2010). The Effect of Immunocontraception on Harem Fidelity in a Feral Horse (*Equus caballus*) Population. Elsevier.

MacFadden, B. J., & Ceding, T. E. (1994). Fossil horses, carbon isotopes and global change. Trends in ecology & evolution, 9(12), 481-486.

McKnight, T. L. (1959). The feral horse in Anglo-America. Geographical review, 506-525.

Morel, M. C. G., McBride, S. D., Chiam, R. S., McKay, A., & Ely, E. (2006). Seasonal variations in physiological and behavioural parameters in a bachelor group of stallion ponies (Equus caballus). *Animal Science*, 82(05), 581-590.

National Academy of Sciences. (2013). Using Science to Improve the BLM Wild Horse and Burro Program: A Way Forward.

Nuñez, Cassandra M.V., Adelman, James S., Mason, Carolyn, Rubenstein, Daniel I. (2009).Immunocontraception Decreases Group Fidelity in a Feral Horse Population Durin the Non-Breeding Season. Elsevier.

Nuñez, Cassandra M.V., Adelman, James S., Rubenstein, Daniel I. (2010). Immunocontraception in Wild Horses (*Equus caballus*) Extends Reproductive Cycling Beyond the Normal Breeding Season. PLOSone.

Nuñez, Cassandra M.V., Adelman, James S., Smith, Jessica, Gesquiere, Laurence R., Rubenstein, Daniel I. (2014). Linking Social Environment and Stress Physiology in Feral Mares (Equus caballus): Group Transfers Elevate Fecal Cortisol Levels. Elsevier.

Ransom, Jason I., Cade, Brian S., Hobbs, N. Thompson. (2010). Influences of Immunocontraception on Time Budgets, Social Behavior, and Body Condition in Feral Horses. Elsevier.

Ransom, Jason I., Hobbs, N. Thompson, Bruemmer, Jason (2013). Contraception Can Lead to Trophic Asynchrony Between Birth Pulse and Resources. PLOSone.

*Ryden, Hope. (1999). *America's Last Wild Horses.* New York: The Lyons Press.

Ransom, Jason I., Powers, Jenny G., Hobbs, N. Thompson, Baker, Dan L. (2014). Ecological Feedbacks Can Reduce Population-Level Efficacy of Wildlife Fertility Control. Journal of Applied Ecology.

*Sadleir RMFS (1969). The Ecology of Reproduction in Wild and Domestic Mammals. London: Methuen & Co. Ltd .. 321 p.

Sharp, Z. D., & Cerling, T. E. (1998). Fossil isotope records of seasonal climate and ecology: straight from the horse's mouth. Geology, 26(3), 219-222.

*Thomas, H. S. (1979). The wild horse controversy. AS Barnes.

Turner Jr, J. W., Liu, I. K., & Kirkpatrick, J. F. (1990). Remotely delivered immunocontraception in captive white-tailed deer. *The Journal of wildlife management*, 154-157.

Turner, John W., Jr., Liu, Irwin K.M., Rutberg, Allen T., Kirkpatrick, Jay F. (1997). Immunocontraception Limits Foal Production in Free-Roaming Feral Horses in Nevada. Wiley.

United States Geological Survey. (2015). Reducing Population Growth Rates: Fertility Control in Wild Horse Mares.

*Indicates a book, which Petitioners have not enclosed with this petition. However, Petitioners can provide a copy of the relevant cited portions if requested.